

14th International HIV Drug Resistance Workshop



7-11 June 2005, Québec City, Canada

SHORT-COURSE COMBIVIR (CBV) SINGLE DOSE NEVIRAPINE REDUCES BUT DOES NOT ELIMINATE THE SELECTION OF NEVIRAPINE-RESISTANT HIV-1: IMPROVED DETECTION BY ALLELE-SPECIFIC PCR

Antivir Ther. 10, Suppl 1:S5 (abstract no. 3)

S Palmer¹✉, V Boltz¹, F Maldarelli¹, N Martinson², J McIntyre², G Gray², Investigators for the trial 14133, M Hopley⁴, T Kimura⁵, D Mayers⁵, P Robinson⁵, J Coffin¹ and J Mellors⁶

¹HIV Drug Resistance Program, NCI, NIH, Frederick, MD, USA; ²Perinatal HIV Research Unit Chris Hani Baragwanath Hospital; and University of the Witwatersrand, Johannesburg, South Africa; ³Study, Investigators, South Africa; ⁴Boehringer Ingelheim ZA, Johannesburg, South Africa; ⁵Boehringer Ingelheim Pharm, Ridgefield, CT, USA; ⁶University of Pittsburgh, Pittsburgh, PA, USA

BACKGROUND: Single-dose nevirapine (sdNVP) to prevent mother-to-child HIV-1 transmission (pMTCT) selects NVP resistant variants in 30–65% of mothers as detected by standard genotyping. The T.O.P.S. trial (BI 1413) is a prospective, randomized three-arm study comparing sdNVP to sdNVP +4 or 7 days of CBV for pMTCT (McIntyre et al., Int. AIDS Cong. 2004). To detect low-frequency selection of NVP-resistant variants in this study, we analysed patient samples with an allele-specific RT-PCR assay that quantifies variants encoding 103N or 181C at frequencies <0.1%.

METHODS: Samples from a subgroup of 32 women were analysed at baseline, 2 and 6 weeks post-therapy from the three treatment arms: sdNVP (10 women) or sdNVP +4 or 7 days of CBV (11 each). Plasma HIV-1 RNA was converted to cDNA, and the target region was amplified and quantified by real-time PCR. This product was used as template for a second round of real-time PCR using discriminatory primers.

RESULTS: Standard genotyping revealed NVP resistance mutations in 70% of women receiving sdNVP at week 2 and 50% at week 6. By contrast, no NVP resistance mutations at codons 103 or 181 were detected by standard genotype at week 2 or 6 among women in this study who received sdNVP +4 or 7 days of CBV. Allele-specific RT-PCR detected 103N or 181C variants in week 6 samples from 75% of women receiving sdNVP alone (mutant frequency 1–75%, median: 7%) and 6 of 22 (27%) of women receiving sdNVP +4 or 7 days of CBV (mutant frequency 0.4–8%, median:

1.4%). There was no difference between the 4 and 7 day CBV arms in the proportion of women with NVP-resistant variants.

CONCLUSIONS: Short-course CBV (4 or 7 days) reduced the selection of NVP-resistant variants following sdNVP from 75% to 27% of women as determined by allele-specific RT-PCR. The selection of low-frequency NVP-resistant variants in the CBV arms was not detected by standard genotype. The impact of these low-frequency NVP-resistant variants on future treatment options is unknown. The optimal duration of CBV to eliminate the selection of NVP-resistant needs to be established.

PRESENTING AUTHOR: S Palmer

2005-06-07

3

Copyright © 2005 - [International Medical Press Ltd.](#) Reproduction of this abstract (other than one copy for personal reference) must be cleared through the International Medical Press Ltd. 2-4 Idol Lane, London EC3R 5DD UK.